REMARKS

Claims 38-47 are now pending, with Claim 38 being the sole independent claim. Claims 25-37 have been cancelled without prejudice to or disclaimer of the subject matter recited therein.

Claims 38-47 have been added. The newly added claims are adequately supported by the original disclosure. Support for the claims can be found throughout the specification and hence it is believed, that no new matter has been added.

Sequence Listing:

In the Office Action of December 31, 2003, the Examiner wrote that "it is unclear what region of SEQ ID NO:3 encodes SEQ ID NO:4." (Office Action, page 2). In response, nucleotides 72 to 1664 of SEQ ID NO:3 encode the 531 amino acid sequence of SEQ ID NO:4. *See e.g.*, Figure 1.

Information Disclosure Statement:

Applicants appreciate the Examiner's consideration of the Form 1449, filed March 5, 2002.

Claim Rejections Under 35 U.S.C. § 112, first paragraph- Written Description:

Claims 25-28 and 31-37 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner contends that "claims reciting 80-95% sequence identity lack adequate written description because Applicant does not disclose a representative number of species as encompassed by these claims." (Office Action, page 2). The Examiner further contends that the "claims encompass mutants and allelic variants and thus imply that structural variants exist in nature, yet no structural variant has been

disclosed" and the claims "encompass Glu-tRNA reductases from other species." (*Id.*, page 2-3.) Further, the Examiner contends that "there is insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine such mutants, allelic variants and Glu-tRNA reductases from other plants and organisms, absent further guidance." (*Id.*, page 3). Applicants respectfully traverse.

Applicants submit that the specification discloses to one of ordinary skill in the art a representative number of Glu-tRNA reductases with at least 80-95% sequence identity to SEQ ID NO:4, and not just a single polynucleotide encoding SEQ ID NO:4.

The specification at page 8, line 6 to page 9, line 9, discloses alterations in nucleotide sequence that are not expected to alter functionality. For example, the specification describes alterations that produce a chemically equivalent amino acid at a given site. It further describes that alterations in the N- or C-terminal portions may be made. (Specification, page 8, lines 21-31.) Thus, from the foregoing and the fact that sequence alignments are readily practiced in the art, the skilled artisan would immediately understand the specification to disclose a representative number of polynucleotide sequences, having different nucleotide substitutions, that encode Glu-tRNA reductase but that vary (within 80% sequence identity) of SEQ ID NO:4. Furthermore, the added claims require at least 95% sequence identity to SEQ ID NO:4; therefore one of ordinary skill is clearly put on notice whether or not a given sequence has at least 95% sequence identity with SEQ ID NO:4.

Second, the Federal Circuit has held that functional descriptions of genetic material can meet the written description requirement if those functional characteristics are "coupled with a known or disclosed correlation between function

and structure, or some combination of such characteristics," *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed.Cir. 2002); *see also* Guidelines, 66 Fed. Reg. at 1106. To meet the requirement, the inventor must "describe the claimed invention so that one skilled in the art can recognize what is claimed." *Id.* at 968.

The present application, the functional characteristic an enzyme and sequence having Glu-tRNA reductase activity. One of ordinary skill in the art is able to test for Glu-tRNA reductase activity using known assays. For example, Applicants refer to the specification, where it states that "assays for Glu-tRNA reductase are presented by Jahn, D. et al. (1991), J. Biol. Chem. 266:2542-2548." (Page 34, lines 12-14).

With respect to structure, the claims require at least 95% sequence identity with the disclosed SEQ ID NO:4. As noted above, sequence alignments are readily practiced in the art; therefore one of ordinary skill is clearly put on notice whether or not a given sequence has at least 95% sequence identity with SEQ ID NO:4. In addition, Applicants kindly invite the Examiner's attention to Bougri et al. (1996, Plant J. 9, 867-878, copy previously submitted). Bougri et al. dislose a wild type and a recombinant barley Glu-tRNA reductase, wherein the recombinant barley Glu-tRNA reductase lacks 19 amino acid residues from the N-terminal of the mature protein. This truncated Glu-tRNA reductase exhibited activity, whereby induced expression rescued an *E. coli* hemA mutant, auxotrophic for 5-aminolevulinate. In addition, Bougri et al. identified a functional divergent barley sequence as indicated in Appendix A (see also below). One skilled in the art would appreciate that the less conserved a residue is, the more likely that it could be modified and function maintained.

Furthermore, Moser et al. (1999, J. Biol. Chem 274, 30679-30693, copy enclosed for Examiner's convenience) disclose a Cys and His residue, involved in the catalytic activity of Glu-tRNA reductases. These residues have been conserved among all Glu-tRNA reductases analyzed to date. One skilled in the art would appreciate that the more highly conserved a residue is, the less likely that it could be modified and function maintained.

Attached hereto as Appendix A is a comparison of SEQ ID NO:4 of the pending claims with Glu-tRNA reductase sequences from barley (NCBI GI No. 2495156) and Methanopyrus kandleri (NCBI GI No. 6102994). Deleted residues of Bougri et al. are shown underlined in Appendix A. Divergent residues are indicted by the respective residue found in the divergent sequence. Residues important for catalytic activity are underlined and in bold. Amino acids conserved among all sequences are indicated with an asterisk (*) on the top row; amino acids conserved only among the barley and corn sequences are indicated by a plus (+); dashes are used by the program to maximize alignment of the sequences.

In view of above discussion, Applicants believe sufficient relevant identifying characteristics have been disclosed to allow one skilled in the art to predictably determine mutants, allelic variants and Glu-tRNA reductases from other plants and organisms. Applicants respectfully request reconsideration and withdrawal of the Section 112, first paragraph rejection for lack of written description.

Claim Rejections Under 35 U.S.C. § 112, first paragraph- Enablement:

Claims 25-28 and 31-37 have been rejected under 35 U.S.C. § 112, first paragraph because, according to the Examiner, the specification does not reasonably provide enablement for nucleic acid sequences having 80-95% sequence identity to SEQ ID NO:4 at the amino acid level. (Office Action, pages 3). The

Examiner contends that "the breadth of the of the claims encompasses sequences having unspecified deletions, additions, substitutions and combinations thereof while maintaining Glu-tRNA reductase activity." (*Id.*) The Examiner further contends that "neither the state of the prior art nor Applicant provided guidance as to which regions of SEQ ID NO:3 or a sequence encoding SEQ ID NO:4 must be retained for activity, and which regions can tolerate mutations." (*Id.*) Applicants respectfully traverse.

Applicants believe that in view of the discussion above, sufficient guidance is provided to one skilled in the art to make and use the claimed invention as commensurate in scope with the claims without undue experimentation. For example, the specification describes alterations that produce a chemically equivalent amino acid at a given site. It further describes that alterations in the N- or C-terminal portions may be made. (Specification, page 8, lines 21-31.) In addition, particular residues are identified by Moser et al. that are likely responsible for activity. Similarly, Bougri et al. disclose regions that are likely more tolerant of substitutions. The Examiner admits that "one skilled in the art can readily make mutations to SEQ ID NO:3 or a sequence encoding SEQ ID NO:4." Hence, one skilled in the art can make and use the claimed invention as commensurate in scope with the claims. Applicants respectfully request reconsideration and withdrawal of the Section 112, first paragraph rejection for lack of enablement.

Claim Rejections Under 35 U.S.C. § 103(a):

Claims 25-27 and 31-37 have been rejected under 35 U.S.C. § 103(a), as being unpatentable over Nakayashiki et al. (1998, Plant Phys., Vol.117:332, Plant Register PGT 98-080) and further in view of Goodman (USPN 4956282 (A)). According to the Examiner, Nakayashiki teaches a sequence having 91.3% sequence identity with SEQ ID NO:4 (Office Action, pages 4-5). Applicants added

claims recite a nucleotide sequence a encoding polypeptide with an amino acid sequence with at least 95% sequence identity to SEQ ID NO:4 or its complement. Applicants believe that this should render the added claims patentable. Applicants respectfully request reconsideration and withdrawal of the Section 103(a) rejection.

Applicants believe that the foregoing is responsive to each of the points recited in the Office Action, and submit that the present application is in allowable form. Favorable consideration and passage to issue are solicited.

Remarks:

The recited Clustal method of alignment uses the default parameters set forth on page 10 of the specification.

Authorization:

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 13-4500, Order No. 2119-4260. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2119-4260. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: June 29, 2004

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APPENDIX A

Comparison of the amino acid sequences of the glutamyl tRNA reductases from corn clone with SID No: csc1c.pk005.i15 (SEQ ID NO:4), the barley sequence set forth in NCBI General Identifier No. 2495156 and the Metahnopyrus kandleri sequence set forth in NCBI General Identifier No. 6102994. Amino acids conserved among all three sequences are indicated by an asterix and sequences identical among the barley and corn sequences are indicated by a plus sign above the conserved residues. Dashes are used by the program to maximize alignment of the sequences. Residues that have been shown to play an important role in the catalytic activity of the glutamyl tRNA reductase from Methanopyrus kandleri (Moser et al.(1999) J. Biol.Chem 274, 30679-30693) are in bold and underlined. Residues, that were deleted from the N-terminal of the mature barley polypeptide, are underlined and those that were found to be divergent in barley are indicated by the respective residue above the alignment (Bougri et al. (1996) Plant J.9, 867-878.

```
            *                                 *  *                            *
            ++  ++++ ++ + +  ++ ++   + +   ++ ++++++++++++ +    +++  ++
SEQ ID NO:4 MATTTSATTAAAAAATTAKPRGSSSALCQR-VAGGGRRRSGVVRCDAAGVEAQAQAVAKA
GI:2495156  MAGATSATAAAGAFAA-AKARGPAAA-CPWLVAAGGRRRSGVVRCDAGG---DAQAASKA
GI:6102994  MED-------------------------LVCVG--------------------ITHKE
                          I                   D
            *    **       *            ***
            ++  +++++++++++++ + ++++++++++++++++++++++++++++++ +++++++
SEQ ID NO:4 ASVAALEQFKISADRYMKERSTIAVIGLSVHTAPVEMREKLAVAEELWPRAIQELTSLNH
GI:2495156  ASITALEQFKISADRYMKEKSSIAVIGLSVHTAPVEMREKLAVAEELWPRAISELTSLNH
GI:6102994  AEVEELEKARFESDEAVRD--IVESFGLS-----------------------------
                                                                    G
                  * **** * *         * *                          * * * ***
            ++++++++++++++++++++++++++++++++++++++++++++++++++++ ++ +++++++
SEQ ID NO:4 IEEAAVLSTCNRMEIYVVALSWNRGIREVVDWMSKKSGIPASELREHLFILRSSDATRHL
GI:2495156  IEEAAVLSTCNRMEIYVVALSWNRGIREVVDWMSKKSGIPASELREHLFMLRDSDATRHL
GI:6102994  --GCVLLQTCNRVEVYA------SGARD-------RAEELGDLIHDDAWVKRGSEAVRHL
                                                          A
            * *  ** *   **  ** ***         * *       *  **  *** * ** **
            ++++++++++++++++++++++++ ++++++++++++++++++++++++ +++++
SEQ ID NO:4 FEVSAGLDSLVLGEGQILAQVKQVVRSGQNSGGLGKNIDRMFKDAITAGKRVRSETNISS
GI:2495156  FEVSAGLDSLVLGEGQILAQVKQVVRNGQNSGGLGKNIDRMFKDAITAGKRVRCETNISA
GI:6102994  FRVACGLESMMVGEQEILRQVKKAYDRAARLGTLDEALKIVFRRAINLGKRAREETRISE

            ****  *******   *     *     *  *** *** * * *   *   * * **  *
            ++++++++++++ +++++++ ++++++++++++++++ +++ +++++++++++++
SEQ ID NO:4 GAVSVSSAAVELALMKLPKSEALSAR-MLLIGAGKMGKLVIKHLVAKGCKKVVVVNRSVE
GI:2495156  GAVSVSSAAVELAMMKLPKSECLSAR-MLLIGAGKMGKLVVKHLIAKGCKKVVVVNRSVE
GI:6102994  GAVSIGSAAVELAEREL---GSLHDKTVLVVGAGEMGKTVAKSLVDRGVRAVLVANRTYE
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```
                                                              A
             *                        *    **    *           * *
             +++++++++++++++++++  ++ +++ +++++++++++  ++ +++++ +++ +  +++
SEQ ID NO:4  RVDAIREEMKDIEIVYRPLSDMYQAAAEADVVFTSTASETSLFAKEHAEALPPVSDTMGG
GI:2495156   RVDAIREEMKDIEIVYRPLTEMYEAAADADVVFTSTASESLLFTKEHAEVLPPISLAMGG
GI:6102994   RAVELARDLGGEAVRFDELVD--HLARSDVVVSATAAPHPVIHVDDVREALR--KRDRRS

                               Q                               A
                  **  ** *           *   ***      * * *          *  **
             +++++++++++++ ++ +++  ++++++++++++++++++++ +++++++++++ ++ ++
SEQ ID NO:4  VRLFVDISVPRNVSACVSEVGAARVYNVDDLKEVVEANKEDRLRKAMEAQTIITEELRRF
GI:2495156   VRLFVDISVPRNVGACLSEVEHARVYNVDDLKEVVEANKEDRVRKAMEAQTIITQELKRF
GI:6102994   PILIIDIANPRDVEEGVENIEDVEVRTIDDLRVIARENLERRRKEIPKVEKLIEEELSTV
                                         D              T
             *     **      **     *       * *       *    **    * **     *
             ++++++++++++++++++++++++++++++++++ +++ + +++++ +++++++++++++
SEQ ID NO:4  EAWRDSLETVPTIKKLRSYADRIRASELEKCLQKVGEDALTKKMRRAIEELSTGIVNKLL
GI:2495156   EAWRDSLETVPTIKKLRSYADRIRASELEKCLQKIGEDNLNKKMRRSIEELSTGIVNKLL
GI:6102994   E---EELE------KLK---ERRLVADVAKSLHEIKDRELERALRR----LKTGDPENVL
                                  D         N
                           *           *          *
             ++++++++++++++++++++++++++++++++++ +++  ++++++++++++
SEQ ID NO:4  HGPLQHLRCDGSDSRTLDETLENMHALNRMFSLDMEKAIIEQKIKAKVEKTQN
GI:2495156   HGPLQHLRCDGSDSRTLDETLENMHALNRMFSLDTEKAVLEQKIKAKVEKTQS
GI:6102994   QD-----FAEAYTKRLINVLTSAIMELPDEYRRAACRALR------RASELNG
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